

Course: INF2178
Assignment: Assignment 4
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Exploring the Interaction Between Visit Time and Group Classification on Normalized Whole Brain Volume in Dementia

Introduction

Alzheimer's disease and other forms of dementia are characterized by progressive neurodegeneration, leading to cognitive decline and functional impairment. Magnetic Resonance Imaging (MRI) plays a crucial role in diagnosing and monitoring these conditions, providing insights into brain structure and volume changes over time. One key metric derived from MRI scans is the normalized whole brain volume (nWBV), which reflects the proportion of brain volume relative to the intracranial volume. Changes in nWBV are indicative of brain atrophy, a hallmark of neurodegenerative diseases, making it an important biomarker for assessing disease progression and the efficacy of therapeutic interventions.

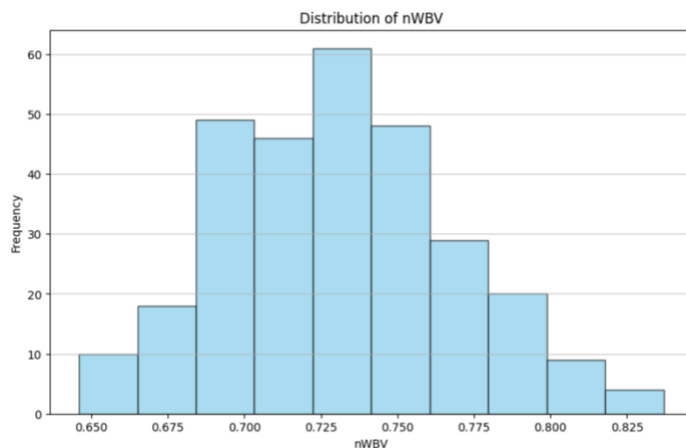
This report aims to explore the relationship between changes in nWBV and various demographic and clinical factors in a cohort of subjects undergoing MRI scans, via implementing statistical analysis, including two-way mixed ANOVA and posthoc test to answer the following research questions:

Research Questions: Whether changes in nWBV from Visit 1 to Visit 2 differ depending on the subject's group classification.

Exploratory Data Analysis

The dataset includes 294 MRI data observations from subjects classified into three groups: Demented, Nondemented, and Converted, with subjects averaging 76 years of age and 14.5 years of education. Most of the dataset records a single visit (mean of 1.49 for the Visit variable), and the follow-up times (MR Delay) vary significantly, ranging from the same day to over 4 years later.

Figure 1. Distribution of nWBV



The histogram of nWBV revealed a near-normal distribution with a central tendency around 0.73, signifying that the most common brain volumes fall within this range. Notably, the slight right skew indicates a subset of the population with higher brain volumes, diverging from the average.

Research Question: Whether changes in nWBV from Visit 1 to Visit 2 differ depending on the subject's group classification?

To address Research Question 1, we focus on whether the change in normalized Whole Brain Volume (nWBV) between two visits is influenced by the dementia-related group to which a subject belongs. The analysis utilized a point plot to visualize the interaction between the within-subject factor of 'Visit' (Visit 1 and Visit 2) and the between-subject factor of 'Group' (Nondemented, Demented, and Converted). The dependent variable under consideration is nWBV.

Figure 2. Distribution of nWBV by Group and Visit

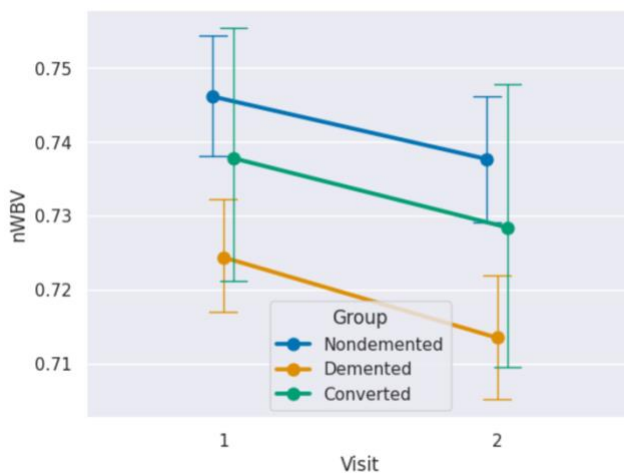


Figure 3. Mean and std by Visit and Group

Visit	Group	Mean	std
1	Converted	0.74	0.03
	Demented	0.72	0.03
	Nondemented	0.75	0.04
2	Converted	0.73	0.04
	Demented	0.71	0.03
	Nondemented	0.74	0.04

The visual (Figure 2) and tabulated data (Figure 3) show a slight decline in nWBV from the first to the second visit across all groups, where the 'Nondemented' group shows a reduction from 0.75 to 0.74, the 'Demented' group from 0.72 to 0.71, and the 'Converted' group from 0.74 to 0.73. These observations underscore a trend of nWBV decrease regardless of dementia status, with 'Nondemented' individuals displaying the highest initial volumes and 'Demented' individuals the lowest. The consistency in variability suggests that the decrease is a common attribute across the cohort, hinting at a potential universal pattern of brain volume shrinkage with aging or disease progression. To determine if the observed changes are significant and not due to random variation, Mixed-ANOVA test and post-hoc test will be conducted.

Mixed-ANOVA Test and Post-hoc test

The ANOVA results reveal a significant effect of 'Visit' ($p < 0.001$, $\eta^2 = 0.401$), indicating that nWBV significantly decreases over time. There's also a significant effect of 'Group' ($p = 0.002$, $\eta^2 = 0.087$), suggesting that nWBV differs between groups. However, the interaction between 'Visit' and 'Group' is not significant ($p = 0.219$, $\eta^2 = 0.021$), indicating that the change in nWBV from Visit 1 to Visit 2 does not significantly differ among the groups.

Figure 4. ANOVA Summary								
Source	SS	DF1	DF2	MS	F	p-unc	np2	eps
Group	0.034	2	141	0.017	6.712	0.002	0.087	Nan

Visit	0.007	1	141	0.007	94.251	0.000	0.401	1.000
Interaction	0.000	2	141	0.000	1.534	0.219	0.021	nan

Post hoc tests highlight that within each group, the decrease in nWBV from Visit 1 to Visit 2 is significant, as shown by the two-sided p-value for 'Visit' ($p < 0.001$). Comparing between groups, the 'Demented' and 'Converted' groups show a significant difference in nWBV at both visits, while the 'Nondemented' group significantly differs from the 'Demented' group at Visit 2.

Figure 5. Post hoc Tests (Parametric = True, Alternative = Two-sided)						
Contrast	Visit	A	B	Paired	alternative	p-unc
Visit	-	1	2	True	Two-sided	0.000
Group	-	Converted	Demented	False	Two-sided	0.182
Group	-	Converted	Nondemented	False	Two-sided	0.527
Group	-	Demented	Nondemented	False	Two-sided	0.000
Visit * Group	1	Converted	Demented	False	Two-sided	0.170
Visit * Group	1	Converted	Nondemented	False	Two-sided	0.648
Visit * Group	1	Demented	Nondemented	False	Two-sided	0.001
Visit * Group	2	Converted	Demented	False	Two-sided	0.205
Visit * Group	2	Converted	Nondemented	False	Two-sided	0.429
Visit * Group	2	Demented	Nondemented	False	Two-sided	0.000

Overall, while there is a general trend of decreasing nWBV over time and differences in nWBV between groups, the rate of this change does not differ statistically between the groups. This suggests that while group categorization is associated with different nWBV levels, the progression rate of brain volume change is consistent across groups.

Power Analysis

To determine the adequacy of our sample size for detecting a significant effect if one exists, a power analysis was conducted. With effect size of 0.7, alpha level of 0.05 (5% Type I error rate), and a power of 0.91 (91% probability of correctly rejecting the null hypothesis), the results indicate that a sample size of approximately 46 subjects (45.45) per group is required to achieve the desired power.

Figure 6. Count of subject by Group	
Group	Count
Nondemented	142
Demented	126
Converted	26

Figure 6 appears that the 'Nondemented' and 'Demented' groups both have enough samples according to the power analysis. However, the 'Converted' group, with only 26 subjects, does not meet the required sample size as determined by the power analysis. This means that while the study is adequately powered for

the 'Nondemented' and 'Demented' groups, it may be underpowered for the 'Converted' group, which could affect the reliability of the findings for that group.

Mixed ANOVA Assumption Check

Assumption: Normal Distribution of Residuals

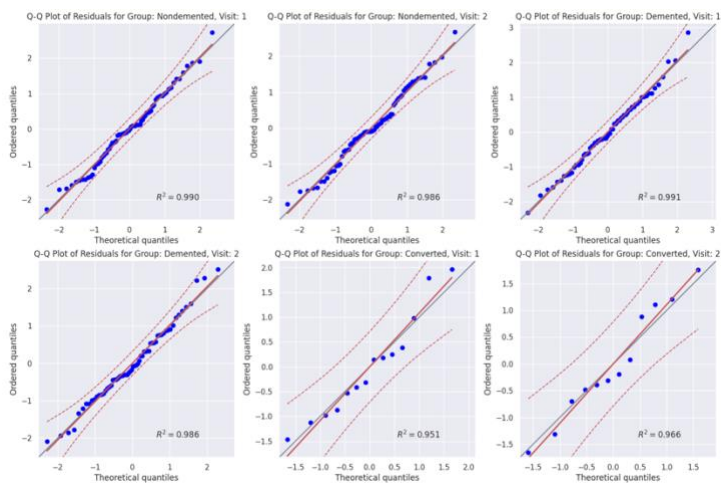


Figure 7. Q-Q plots of residuals

The Q-Q plots indicate that residuals for the Nondemented and Demented groups at both visits conform closely to a normal distribution, with high R² values. The Converted group shows slight deviations but generally adheres to normality, supporting the validity of the ANOVA assumptions for the dataset.

Assumption: Homogeneity of variances

Figure 8. Levene’s Test		
W	pval	Equal_var
0.530546	0.753099	True

The test result yields a p-value of 0.753, greater than alpha level of 0.05, we fail to reject the null hypothesis of Levene's test, which means there is no

evidence to suggest that the variances are unequal. This implies that the assumption of homogeneity of variances is met for the dataset, validating the use of ANOVA for further analysis.

Conclusion

In conclusion, the analysis addressed the research question by determining that the rate of change in normalized Whole Brain Volume (nWBV) from Visit 1 to Visit 2 does not differ significantly across the Nondemented, Demented, and Converted groups. While each group exhibited a slight decline in nWBV, indicating brain volume reduction over time, the mixed ANOVA revealed no significant interaction effect, implying that these changes occurred at a similar pace regardless of group classification. These findings suggest that the group status, in terms of dementia progression, does not uniquely influence the trajectory of nWBV reduction over the time frame studied.